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PATENT

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March 29, 2006  
Date

Kay Bulen  
Kay Bulen

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Tim Hui-Ming Huang  
Application No. : 10/081,327  
Filed : 02-21-2002  
For : HIGH-THROUGHPUT METHODS FOR DETECTING DNA  
METHYLATION  
Examiner : Jeanine Anne Goldberg  
Art Unit : 1634  
Docket No. : 40629-2  
Date : March 29, 2006  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Dear Commissioner:

In accordance with 37 C.F.R. §§ 1.56 and 1.97 through 1.98, applicant wishes to make known to the Patent and Trademark Office the references set forth on the attached form PTO/SB/08. This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior Application No. 09/497,855, filed February 4, 2000 (now U.S. 6,604,432). The references listed on the attached form PTO/SB/08 were submitted to and/or cited by the Patent and Trademark Office in this prior application. As to any reference supplied, applicant does not admit that it is "prior art" under 35 U.S.C. §§ 102 or 103, and specifically reserves the right to traverse or antedate any such reference, as by a showing under 37 C.F.R. § 1.131 or other method. Although the aforesaid references are made known to the Patent and Trademark Office in

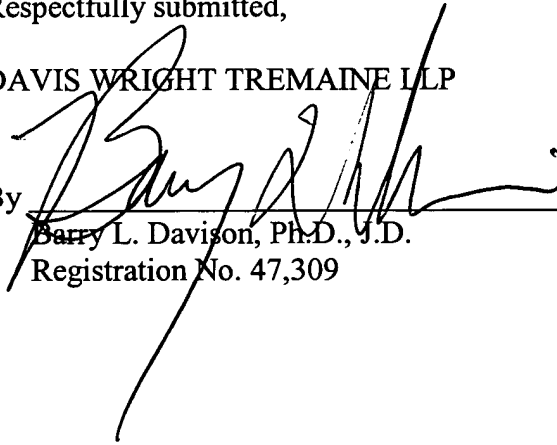
compliance with applicant's duty to disclose all information he/she is aware of which is believed relevant to the examination of the above-identified application, applicant believes that his/her invention is patentable.

Please acknowledge receipt of this Information Disclosure Statement and kindly make the cited references of record in the above-identified application. No fee is deemed due, but if necessary, the Commissioner is authorized to charge any additional fees due and to credit any overpayments to Deposit Account No. 04-0258 of Davis Wright Tremaine LLP. A copy of this sheet is enclosed.

Respectfully submitted,

DAVIS WRIGHT TREMAINE LLP

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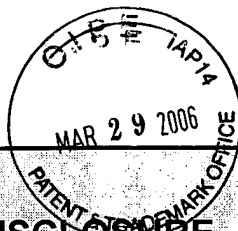
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Substitute for form 1449/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>				Application Number	10/081,327
				Filing Date	02-21-2002
				First Named Inventor	Huang
				Art Unit	1634
				Examiner Name	Jeanine Anne Goldberg
Sheet	1	of	2	Attorney Docket Number	40629-2

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	US-4,682,195	07-21-1987	Yilmaz	
	A2	US-4,683,202	07-28-1987	Mullis	
	A3	US-4,800,159	01-24-1989	Mullis et al.	
	A4	US-5,589,339	12-31-1996	Hampson et al.	
	A5	US-5,591,575	01-07-1997	Hampson et al.	
	A6	US-5,786,146	07-28-1998	Herman et al.	
	A7	US-5,871,917	02-16-1999	Duffy	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
	A8	AKOPYANTS et al., "PCR-based Subtractive Hybridization and Differences in Gene Content Among Strains of <i>Helicobacter pylori</i> ", Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 13108-13113, 1998			
	A9	ANTEQUERA, F., et al., "High Levels of De Novo Methylation and Altered Chromatin Structure at CpG Islands in Cell Lines", Cell, Vol. 2, pp. 503-514, 1990			
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	A11	BAYLIN, STEPHEN B., "Tying it all Together: Epigenetics, Genetics, Cell Cycle, and Cancer", Science, Vol. 277, pp. 1948-1949, 1997			
	A12	BELINSKY et al., "Aberrant Methylation of <i>p16<sup>INK4a</sup></i> is an Early Event in Lung Cancer and a Potential Biomarker for Early Diagnosis", Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 11891-11896, 1998			
	A13	BELINSKY et al., "Increased Cytosine DNA-methyltransferase Activity is Target-cell-specific and an Early Event in Lung Cancer", Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 4045-4050, 1996			
	A14	BLOOM, H.J.G. AND RICHARDSON, W.W., "Histological Grading and Prognosis in Breast Cancer", British Journal of Cancer, Vol. 11, pp. 359-377, 1957			
	A15	BRANDEIS, M. et al., "Sp1 Elements Protect a CpG Island from <i>de novo</i> Methylation", Nature, Vol. 371, pp. 435-438, 1994			
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	A17	CHRISTMAN et al., "5-Methyl-2'-deoxycytidine in single-stranded DNA can act in cis to Signal <i>de novo</i> DNA Methylation", Proc. Natl. Acad. Sci., USA, Vol. 92, pp. 7347-7351, 1995			
	A18	CHUANG et al., "Human DNA-(Cytosine-5) Methyltransferase-PCNA Complex as a Target for <i>p21<sup>WAF1</sup></i> ", Science, Vol. 277, pp. 1996-2000, 1997			
	A19	CRAIG et al., "Removal of Repetitive Sequences from FISH Probes Using PCR-Assisted Affinity Chromatography", Hum. Genet., Vol. 100, pp. 472-476, 1997			
	A20	CROSS et al., "Purification of CpG Islands Using a Methylated DNA Binding Column", Nature Genet., Vol. 6, pp. 236-244, 1994			
	A21	FROMMER, M. et al., "A Genomic Sequencing Protocol that Yields a Positive Display of 5-Methylcytosine Residues in Individual DNA strands", Proc. Natl. Acad. Sci. USA, Vol. 89, pp. 1827-1831, 1992			
	A22	GRAFF et al., "Mapping Patterns of CpG Island Methylation in Normal and Neoplastic Cells Implicates Both Upstream and Downstream Regions in <i>de Novo</i> Methylation", J. Biol. Chem., Vol. 272, No. 35, pp. 22322-22329, 1997			



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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

**Complete if Known**

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Examiner Name	Jeanine Anne Goldberg
Attorney Docket Number	40629-2

Sheet	2	of	2
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**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	A23	HERMAN et al., "Methylation-specific PCR: A Novel PCR Assay for Methylation Status of CpG Islands", Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 9821-9826, 1996	
	A24	HUANG, T.H., et al., "Methylation Profiling of CpG Islands in Human Breast Cancer Cells", Human Molecular Genetics, Vol. 8, No. 3, pp. 459-470, 1999	
	A25	JONES, P.A., "DNA Methylation Errors and Cancer", Cancer Res., Vol. 56, pp. 2463-2467, 1996	
	A26	LAIRD et al., "DNA Methylation and Cancer", Hum. Mol. Genet., Vol. 3, pp. 1487-1495, 1994	
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	A28	LI et al., "Role for DNA Methylation in Genomic Imprinting", Nature, Vol. 366, pp. 362-365, 1993	
	A29	MUMMANENI, P., et al., "Epigenetic Gene Inactivation Induced by a Cis-acting Methylation Center", J. Biol. Chem., Vol. 270, No. 2, pp. 788-792, 1995	
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	A32	SCHENA et al., "Quantitative Monitoring of Gene Expression Patterns with a Complementary DNA Microarray", Science, Vol. 270, pp. 467-470, 1995	
	A33	SINGER-SAM, J. and RIGGS, A.D., "X-Chromosome Inactivation and DNA Methylation", DNA Methylation: Molecular Biology and Biological Significance, pp. 358-384, 1993	
	A34	VERTINO et al., "De Novo Methylation of CpG Island Sequences in Human Fibroblasts Overexpressing DNA (Cytosine-5) - Methyltransferase", Mol. Cell Biol., Vol. 16, pp. 4555-4565, 1996	
	A35	WU et al., "Expression of Prokaryotic HhaI DNA Methyltransferase is Transforming and Lethal to NIH 3T3 Cells", Cancer Res., Vol. 56, pp. 616-622, 1996	

Examiner Signature	Date Considered
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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